Novel site-specific mast cell subpopulations in the human lung

Cecilia Andersson, PhD student
Respiratory Medicine and Allergology
Airway Inflammation
Lund University
MAST CELL HISTORY

Mast cells (~15 μm in diameter)
- Paul Ehrlich in 1878
- Bone marrow precursor
- Mature in tissue
- Prominent near the boundaries between the outside world and the internal milieu

Ciona intestinalis
- Ancestor of vertebrates 550 million years ago
- Connective tissue mast cells
- Host defense
**Histology-based Techniques**

- Immunohistochemistry
- Confocal Laser Microscopy
- Laser Capture Microscopy
- In Situ hybridisation
- TUNEL technique
- Receptor Autoradiography
- Transmissions electron microscopy
- Scanning electron Microscopy
- "Virtual Microscopy"
- State-of-the-Art Computerized Image Analysis

**Validated Human Tissue Samples**

**ASTHMA**
- Healthy controls
- Controls + Rhinitis
- Mild Asthma
- Moderate Asthma
- Uncontrolled ST Asthma
- Controlled ST Asthma
- Severe Asthma
- Fatal Asthma

**COPD**
- Non-smoking controls
- Smoking controls
- GOLD 1
- GOLD 2
- GOLD 3
- GOLD 4

**Cystic Fibrosis**
- Severe CF
- Mid-Stage CF
- IPF
- Severe IPF

**Respir Infections**
- Rhinovirus
- Adenovirus
- RSV
- Influenza A

**Collaborations with:**
- Dept Thoracic Surg, Lund
- Dept Respir Med, Lund
- AZ, Lund
- Aarhus, Denmark
- FDA, Washington, USA
- New York, USA
- Sao Paulo, Brazil
- Santiago, Chile
- Mexico City, Mexico
- Shanghai, China (Pittsburg, USA)
Examples of site-specific $MC_{TC}$ populations in human lungs
MC heterogeneity, under human *in vivo* condition, is poorly investigated.

We show that under base-line conditions each anatomical compartment contains distinct MC$_T$ and MC$_{TC}$ populations.

This should be taken under consideration when quantifying lung derived mast cells *in vitro* and when purifying mast cells without proper knowledge of the original tissue source.
MAST CELL-ASSOCIATED ALVEOLAR INFLAMMATION IN ATOPIC UNCONTROLLED ASTHMA

- A significant proportion of patients with asthma remain symptomatic despite treatment with inhaled glucocorticosteroids (ICS).
- In these patients, virtually no information exists on inflammatory status in peripheral lung tissues.
- This study explores the hypothesis that a peripheral mast cell involvement is present in symptomatic patients treated with ICS.

- Bronchial and transbronchial biopsies
- 10 atopic symptomatic asthmatics on ICS
- 8 healthy controls.
Density of FcεRI and IgE Positive Mast Cells in Alveolar Parenchyma

→ 50 fold increase!

→ 600 fold increase!

Andersson et al. JACI resubmitted 2010.
Uncontrolled Asthma - Conclusions

- The present study shows that in patients with uncontrolled steroid-treated asthma there is an infiltration of mast cells with increased expression of the high-affinity IgE-receptor in the distal airways.

- These findings may have clinical implications and underscore the need to target peripheral lung inflammation in this patient group.

- The increased IgE-receptor expression might be specific for uncontrolled asthma since we could not detect this phenomenon in COPD, CF, IPF or fatal asthma.